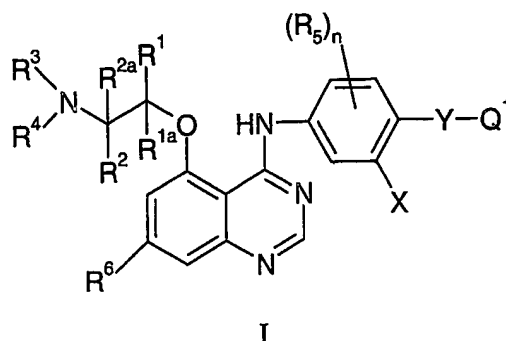


CLAIMS

1. A quinazoline derivative of the formula I:



5 wherein:

each of R^1 and R^2 , which may be the same or different, is selected from hydrogen, carboxy, cyano, formyl, (1-3C)alkyl, (2-3C)alkanoyl, (1-3C)alkoxycarbonyl, carbamoyl, N-(1-3C)alkylcarbamoyl and N, N-di-[(1-3C)alkyl]carbamoyl;

each of R^{1a} and R^{2a} , which may be the same or different, is selected from hydrogen and (1-3C)alkyl;

each of R^3 and R^4 , which may be the same or different, is selected from hydrogen, (1-3C)alkyl and (2-4C) alkenyl;

and wherein any CH or CH₂ or CH₃ within any of R^1 , R^{1a} , R^2 , R^{2a} , R^3 and R^4 optionally bears on each said CH or CH₂ or CH₃ one or more (for example 1, 2 or 3) halogeno substituents or a substituent selected from hydroxy, cyano, (1-3C)alkoxy, amino, (2-3C)alkanoyl, (1-3C)alkylamino and di-[(1-3C)alkyl]amino;

X is selected from hydrogen, halogeno, (1-4C)alkyl, (1-4C)alkoxy, (2-4C)alkenyl and (2-4C)alkynyl;

each R^5 , which may be the same or different, is selected from halogeno, hydroxy, (1-4C)alkyl, (1-4C)alkoxy, (2-4C)alkenyl and (2-4C)alkynyl;

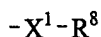
Y is selected from a direct bond, O, S, OC(R^7)₂, SC(R^7)₂, SO, SO₂, N(R^7), CO and N(R^7)C(R^7)₂ wherein each R^7 is, independently, hydrogen or (1-6C)alkyl;

Q^1 is selected from phenyl, pyridyl, pyrazinyl, 1,3-thiazolyl, 1H-imidazolyl, 1H-pyrazolyl, 1,3-oxazolyl and isoxazolyl,

and wherein Q^1 optionally bears one or more substituents (for example 1, 2 or 3), which may be the same or different, selected from halogeno, cyano, nitro, hydroxy, amino, carboxy, carbamoyl, sulfamoyl, formyl, mercapto, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (1-6C)alkylsulfanyl,

-120-

(1-6C)alkylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, (3-6C)alkenoylamino, N-(1-6C)alkyl-(3-6C)alkenoylamino, (3-6C)alkynoylamino, N-(1-6C)alkyl-(3-6C)alkynoylamino, N-(1-6C)alkylsulfamoyl, N,N-di-[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino, and N-(1-6C)alkyl-(1-6C)alkanesulfonylamino, or from a group of the formula:



wherein X^1 is a direct bond or is selected from O, CO and $N(R^9)$, wherein R^9 is hydrogen or (1-6C)alkyl, and R^8 is halogeno-(1-6C)alkyl, hydroxy-(1-6C)alkyl, carboxy-(1-6C)alkyl, (1-6C)alkoxy-(1-6C)alkyl, cyano-(1-6C)alkyl, amino-(1-6C)alkyl, N-(1-6C)alkylamino-(1-6C)alkyl, N,N-di-[(1-6C)alkyl]amino-(1-6C)alkyl, (2-6C)alkanoylamino-(1-6C)alkyl, (1-6C)alkoxycarbonylamino-(1-6C)alkyl, carbamoyl-(1-6C)alkyl, N-(1-6C)alkylcarbamoyl-(1-6C)alkyl, N,N-di-[(1-6C)alkyl]carbamoyl-(1-6C)alkyl, (2-6C)alkanoyl-(1-6C)alkyl or (1-6C)alkoxycarbonyl-(1-6C)alkyl,

and wherein any CH_2 or CH_3 within a substituent on Q^1 optionally bears on each said CH_2 or CH_3 one or more (for example 1, 2, or 3) halogeno or (1-6C)alkyl substituents or a substituent selected from hydroxy, cyano, amino, (1-4C)alkoxy, (1-4C)alkylamino and di-[(1-4C)alkyl]amino;

R^6 is selected from hydrogen, (1-6C)alkoxy, (2-6C)alkenyloxy and (2-6C)alkynyloxy,

and wherein any CH_2 or CH_3 group within a R^6 substituent optionally bears on each said CH_2 or CH_3 group one or more halogeno or (1-6C)alkyl substituents, or a substituent selected from hydroxy and (1-6C)alkoxy;

n is 0, 1, 2 or 3;

or a pharmaceutically acceptable salt thereof.

2. A quinazoline derivative of the formula I as defined in claim 1, wherein R^1 is selected from hydrogen, methyl and ethyl, R^2 is selected from hydrogen, carboxy, cyano, methyl, ethyl, acetyl, methoxycarbonyl, carbamoyl, N-methylcarbamoyl and N,N-dimethylcarbamoyl, and R^{1a} and R^{2a} are each hydrogen.

3. A quinazoline derivative of the formula I as defined in claim 1, wherein R^2 is selected from hydrogen, methyl and ethyl, R^1 is selected from hydrogen, carboxy, cyano, methyl, ethyl, acetyl, methoxycarbonyl, carbamoyl, N-methylcarbamoyl and N, N-di-methylcarbamoyl, and R^{1a} and R^{2a} are each hydrogen.
- 5
4. A quinazoline derivative of the formula I as defined in claim 1, wherein R^1 and R^{1a} are each hydrogen, R^2 is selected from hydrogen, carboxy, cyano, methyl, ethyl, acetyl, methoxycarbonyl, carbamoyl, N-methylcarbamoyl and N, N-di-methylcarbamoyl, and R^{2a} is selected from hydrogen and (1-3C)alkyl.
- 10
5. A quinazoline derivative of the formula I as defined in claim 1, wherein R^2 and R^{2a} are each hydrogen, R^1 is selected from hydrogen, carboxy, cyano, methyl, ethyl, acetyl, methoxycarbonyl, carbamoyl, N-methylcarbamoyl and N, N-di-methylcarbamoyl, and R^{1a} is selected from hydrogen and (1-3C)alkyl.
- 15
6. A quinazoline derivative of the formula I as defined in any one of claims 1, 2, 3 and 5, wherein R^1 is methyl, and R^2 , R^{1a} and R^{2a} are each hydrogen.
7. A quinazoline derivative of the formula I as defined in any one of claims 1 to 4,
- 20 wherein R^2 is methyl and R^1 , R^{1a} and R^{2a} are each hydrogen.
8. A quinazoline derivative of the formula I as defined in claim 1 or claim 5, wherein R^1 and R^{1a} are each methyl and R^2 and R^{2a} are each hydrogen.
- 25 9. A quinazoline derivative of the formula I as defined in claim 1 or claim 4, wherein R^2 and R^{2a} are each methyl and R^1 and R^{1a} are each hydrogen.
10. A quinazoline derivative of the formula I as defined in any one of the preceding claims, wherein each of R^3 and R^4 , which may be the same or different, is selected from (1-3C)alkyl, wherein any CH or CH_2 or CH_3 within any of R^3 and R^4 optionally bears on each said CH or CH_2 or CH_3 one or more substituents selected from hydroxy and (1-3C)alkoxy.
- 30

11. A quinazoline derivative of the formula I as defined in any one of claims 1 to 9, wherein each of R³ and R⁴, which may be the same or different, is selected from hydrogen, methyl, ethyl, propenyl, 2-methoxyethyl and 2-hydroxyethyl.
- 5 12. A quinazoline derivative of the formula I as defined in claim 11, wherein each of R³ and R⁴, which may be the same or different, is selected from methyl, ethyl, propenyl, 2-methoxyethyl and 2-hydroxyethyl.
13. A quinazoline derivative of the formula I as defined in claim 11 or claim 12, wherein
10 R³ is methyl and R⁴ is selected from methyl, ethyl, 2-hydroxyethyl, 2-methoxyethyl and propenyl.
14. A quinazoline derivative of the formula I as defined in any one of claims 10 to 13, wherein R³ and R⁴ are each methyl.
- 15
15. A quinazoline derivative of the formula I as defined in any one of claims 10 to 12, wherein R³ is ethyl and R⁴ is 2-hydroxyethyl.
16. A quinazoline derivative of the formula I as defined in any one of the preceding
20 claims, wherein X is selected from hydrogen, halogeno, (1-4C)alkyl and (1-4C)alkoxy.
17. A quinazoline derivative of the formula I as defined in claim 16, wherein X is selected from hydrogen, fluoro, chloro, methyl and methoxy.
- 25 18. A quinazoline derivative of the formula I as defined in claim 16 or claim 17, wherein X is selected from methyl and chloro.
19. A quinazoline derivative of the formula I as defined in claim 18, wherein X is chloro.
- 30 20. A quinazoline derivative of the formula I as defined in claim 18, wherein X is methyl.

21. A quinazoline derivative of the formula I as defined in any one of the preceding claims, wherein Y is selected from O, S and $\text{OC(R}^7\text{)}_2$ wherein each R^7 is, independently, hydrogen or (1-4C)alkyl.
- 5 22. A quinazoline derivative of the formula I as defined in claim 21, wherein Y is selected from O, S and OCH_2 .
23. A quinazoline derivative of the formula I as defined in claim 21 or claim 22, wherein Y is O.
- 10 24. A quinazoline derivative of the formula I as defined in claim 21 or claim 22, wherein Y is S.
25. A quinazoline derivative of the formula I as defined in claim 21 or claim 22, wherein
15 Y is OCH_2 .
26. A quinazoline derivative of the formula I as defined in any one of the preceding claims, wherein n is 0.
- 20 27. A quinazoline derivative of the formula I as defined in any one of the preceding claims, wherein Q^1 is selected from phenyl, 2-pyridyl, 2-pyrazinyl, 1,3-thiazol-4-yl, 1,3-thiazol-5-yl, 1H-imidazol-2-yl and isoxazol-3-yl, and wherein Q^1 optionally bears one or more substituents, which may be the same or different, as defined in claim 1.
- 25 28. A quinazoline derivative of the formula I as defined in claim 27, wherein Q^1 is selected from phenyl, 2-pyridyl, 2-pyrazinyl, 1,3-thiazol-4-yl, 1,3-thiazol-5-yl, 1H-imidazol-2-yl and 3-isoxazolyl, and wherein Q^1 optionally bears one or more substituents, which may be the same or different, selected from fluoro and (1-4C)alkyl.
- 30 29. A quinazoline derivative of the formula I as defined in claim 27 or claim 28, wherein Q^1 is selected from 3-fluorophenyl, 2-pyridyl, 2-pyrazinyl, 1-methyl-1H-imidazol-2-yl, 1,3-thiazol-4-yl, 1,3-thiazol-5-yl and 5-methyl-3-isoxazolyl.

30. A quinazoline derivative of the formula I as defined in any one of the preceding claims, wherein R⁶ is hydrogen.
31. A quinazoline derivative selected from one or more of the following:
- 5 4-(3-Chloro-4-(2-pyridylmethoxy)anilino)-5-(2dimethylaminoethoxy)quinazoline;
4-(3-Chloro-4-(2-pyridylmethoxy)anilino)-5-(2-dimethylamino-1-methylethoxy)quinazoline;
4-(3-Chloro-4-(1-methyl-1*H*-imidazol-2-ylthio)anilino)-5-(2-dimethylaminoethoxy)quinazoline;
4-(3-Chloro-4-(1-methyl-1*H*-imidazol-2-ylthio)anilino)-5-(2-dimethylamino-2-
10 methylethoxy)quinazoline;
4-(4-(3-Fluorobenzoyloxy)anilino)-5-(2-dimethylaminoethoxy)quinazoline;
4-(4-(3-Fluorobenzoyloxy)anilino)-5-(2-dimethylamino-1-methylethoxy)quinazoline;
4-(3-Chloro-4-(2-pyrazinylmethoxy)anilino)-5-(2-dimethylaminoethoxy)quinazoline;
4-(3-Chloro-4-(2-pyrazinylmethoxy)anilino)-5-(2-dimethylamino-1-
15 methylethoxy)quinazoline;
4-(3-Chloro-4-(5-methylisoxazol-3-ylmethoxy)anilino)-5-(2-dimethylaminoethoxy)quinazoline;
4-(3-Chloro-4-(5-methylisoxazol-3-ylmethoxy)anilino)-5-(2-dimethylamino-1-methylethoxy)quinazoline;
20 4-(3-Chloro-4-(3-fluorobenzoyloxy)anilino)-5-(2-(*N*-ethyl-*N*-methylamino)ethoxy)quinazoline;
4-(3-Chloro-4-(3-fluorobenzoyloxy)anilino)-5-(2-dimethylaminoethoxy)quinazoline;
4-(3-Chloro-4-(3-fluorobenzoyloxy)anilino)-5-[2-(*N*-(2-hydroxyethyl)-*N*-methylamino)ethoxy]quinazoline;
25 4-(3-Chloro-4-(2-pyridylmethoxy)anilino)-5-(2-(*N*-ethyl-*N*-methylamino)ethoxy)quinazoline;
4-(3-Chloro-4-(2-pyridylmethoxy)anilino)-5-(2-(*N*-(2-hydroxyethyl)-*N*-methylamino)ethoxy)quinazoline;
4-(3-Chloro-4-(3-fluorobenzoyloxy)anilino)-5-(2-dimethylamino-2-methylethoxy)quinazoline;
30 4-(3-Chloro-4-(2-pyridylmethoxy)anilino)-5-(2-dimethylamino-2-methylethoxy)quinazoline;
N-[3-Chloro-4-(1,3-thiazol-4-ylmethoxy)phenyl]-5-[2-(dimethylamino)ethoxy]quinazolin-4-amine;
N-[3-Chloro-4-(pyridin-2-yloxy)phenyl]-5-[2-(dimethylamino)ethoxy]quinazolin-4-amine;

- N*-[3-Chloro-4-(1,3-thiazol-4-ylmethoxy)phenyl]-5-[(1*R*)-2-(dimethylamino)-1-methylethoxy]quinazolin-4-amine;
- N*-[3-Chloro-4-(pyrazin-2-ylmethoxy)phenyl]-5-[(1*R*)-2-(dimethylamino)-1-methylethoxy]quinazolin-4-amine;
- 10 *N*-{3-Chloro-4-[(3-fluorobenzyl)oxy]phenyl}-5-[(1*R*)-2-(dimethylamino)-1-methylethoxy]quinazolin-4-amine;
- N*-[3-Chloro-4-(pyridin-2-ylmethoxy)phenyl]-5-[2-(dimethylamino)-2-methylpropoxy]quinazolin-4-amine;
- 15 *N*-[3-Chloro-4-(1,3-thiazol-4-ylmethoxy)phenyl]-5-[2-(dimethylamino)-2-methylpropoxy]quinazolin-4-amine;
- N*-{3-Chloro-4-[(5-methylisoxazol-3-yl)methoxy]phenyl}-5-[2-(dimethylamino)-2-methylpropoxy]quinazolin-4-amine;
- 5-[2-(Dimethylamino)ethoxy]-*N*-[3-methyl-4-(pyridin-2-ylmethoxy)phenyl]quinazolin-4-
- 20 amine;
- 5-[2-(Dimethylamino)ethoxy]-*N*-[3-methyl-4-(1,3-thiazol-4-ylmethoxy)phenyl]quinazolin-4-amine;
- 5-[2-(Dimethylamino)ethoxy]-*N*-{3-methyl-4-[(5-methylisoxazol-3-yl)methoxy]phenyl}quinazolin-4-amine;
- 25 5-[(1*R*)-2-(Dimethylamino)-1-methylethoxy]-*N*-[3-methyl-4-(pyridin-2-ylmethoxy)phenyl]quinazolin-4-amine;
- 5-[(1*R*)-2-(Dimethylamino)-1-methylethoxy]-*N*-[3-methyl-4-(pyrazin-2-ylmethoxy)phenyl]quinazolin-4-amine;
- 5-[(1*R*)-2-(dimethylamino)-1-methylethoxy]-*N*-[3-methyl-4-(1,3-thiazol-4-
- 30 ylmethoxy)phenyl]quinazolin-4-amine;
- 5-[(1*R*)-2-(Dimethylamino)-1-methylethoxy]-*N*-{3-methyl-4-[(5-methylisoxazol-3-yl)methoxy]phenyl}quinazolin-4-amine;

N-[3-Chloro-4-(pyrazin-2-ylmethoxy)phenyl]-5-[(1*S*)-2-(dimethylamino)-1-methylethoxy]quinazolin-4-amine;

N-[3-Chloro-4-[(3-fluorobenzyl)oxy]phenyl]-5-[(1*S*)-2-(dimethylamino)-1-methylethoxy]quinazolin-4-amine;

- 5 *N*-[3-Chloro-4-(pyridin-2-ylmethoxy)phenyl]-5-[(1*R*)-2-(dimethylamino)-1-methylethoxy]quinazolin-4-amine;

N-[3-Chloro-4-(3-chlorophenyl)-4-methoxyphenyl]-5-[(1*R*)-2-(dimethylamino)-1-

- 5-[2-(dimethylamino)-2-methylpropoxy]-*N*-[3-methyl-4-(1,3-thiazol-4-ylmethoxy)phenyl]quinazolin-4-amine;
- 5-[2-(Dimethylamino)ethoxy]-*N*-{3-methoxy-4-[(5-methylisoxazol-3-yl)methoxy]phenyl}quinazolin-4-amine;
- 5 5-[2-(Dimethylamino)ethoxy]-*N*-[3-methoxy-4-(pyrazin-2-ylmethoxy)phenyl]quinazolin-4-amine;
- 5-[2-(Dimethylamino)ethoxy]-*N*-[3-fluoro-4-(1,3-thiazol-5-ylmethoxy)phenyl]quinazolin-4-amine;
- N*-[3-Chloro-4-(pyridin-2-ylmethoxy)phenyl]-5-[(1*S*)-2-(dimethylamino)-1-methylethoxy]quinazolin-4-amine;
- 10 *N*-[3-Chloro-4-(pyridin-2-ylmethoxy)phenyl]-5-[(2*S*)-2-(dimethylamino)propyl]oxy}quinazolin-4-amine;
- N*-[3-Chloro-4-(pyridin-2-ylmethoxy)phenyl]-5-[(2*R*)-2-(dimethylamino)propyl]oxy}quinazolin-4-amine;
- 15 5-[2-[Allyl(methyl)amino]ethoxy]-*N*-[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]quinazolin-4-amine;
- 2-[[2-[(4-[[3-Chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]ethyl](ethyl)amino]ethanol;
- N*-[3-Chloro-4-(pyridin-2-ylmethoxy)phenyl]-5-[(1*S*)-2-[(2-methoxyethyl)(methyl)amino]-1-methylethoxy}quinazolin-4-amine;
- 20 *N*-[3-Chloro-4-(pyridin-2-ylmethoxy)phenyl]-5-[(1*R*)-2-[ethyl(methyl)amino]-1-methylethoxy}quinazolin-4-amine;
- 5-[(1*R*)-2-[Allyl(methyl)amino]-1-methylethoxy]-*N*-[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]quinazolin-4-amine;
- 25 5-[(1*S*)-2-[Allyl(methyl)amino]-1-methylethoxy]-*N*-[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]quinazolin-4-amine;
- N*-{3-Chloro-4-[(3-fluorobenzyl)oxy]phenyl}-5-[(2*S*)-2-(dimethylamino)propyl]oxy}quinazolin-4-amine;
- N*-{3-Chloro-4-[(3-fluorobenzyl)oxy]phenyl}-5-[(2*R*)-2-(dimethylamino)propyl]oxy}quinazolin-4-amine;
- 30 (dimethylamino)propyl]oxy}quinazolin-4-amine;
- N*-{3-Chloro-4-[(1-methyl-1*H*-imidazol-2-yl)thio]phenyl}-5-[(2*S*)-2-(dimethylamino)propyl]oxy}quinazolin-4-amine;

- N*-{3-Chloro-4-[(1-methyl-1*H*-imidazol-2-yl)thio]phenyl}-5-[[*(2R)*-2-(dimethylamino)propyl]oxy]quinazolin-4-amine;
- N*-{3-Chloro-4-[(1-methyl-1*H*-imidazol-2-yl)thio]phenyl}-5-[(*1R*)-2-(dimethylamino)-1-methylethoxy]quinazolin-4-amine;
- 5 5-[2-(Dimethylamino)-1-methylethoxy]-*N*-(3-methoxy-4-phenoxyphenyl)quinazolin-4-amine;
- 5-[2-(Dimethylamino)-1-methylethoxy]-*N*-(3-methoxy-4-phenoxyphenyl)quinazolin-4-amine;
- and
- N*-[3-Chloro-4-(pyridin-2-ylmethoxy)phenyl]-5-[2-(dimethylamino)-1,1-dimethylethoxy]quinazolin-4-amine;
- 10 or a pharmaceutically acceptable salt thereof.

32. A pharmaceutical composition which comprises a quinazoline derivative of the formula I, or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1 to 31 in association with a pharmaceutically-acceptable diluent or carrier.

15

33. A quinazoline derivative of the formula I, or a pharmaceutically-acceptable salt thereof, as defined in any one of claims 1 to 31 for use as a medicament.

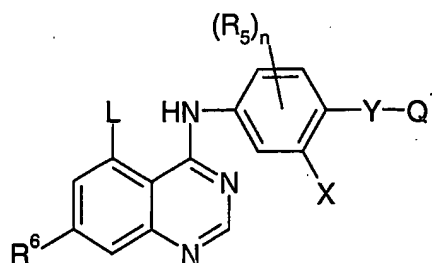
34. A quinazoline derivative of the formula I, or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1 to 31 for use in the production of an anti-proliferative effect which effect is produced alone or in part by inhibiting erbB2 receptor tyrosine kinase in a warm-blooded animal such as man.

35. A quinazoline derivative of the formula I, or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1 to 31 for use in the production of an erbB2 receptor tyrosine kinase inhibitory effect in a warm-blooded animal such as man.

36. A quinazoline derivative of the formula I, or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1 to 31 for use in the production of a selective erbB2 receptor tyrosine kinase inhibitory effect in a warm-blooded animal such as man.

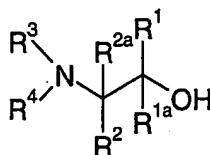
37. A process for the preparation of a quinazoline derivative of the formula I, or a pharmaceutically acceptable salt thereof, as defined in claim 1 which comprises:

(a) the reaction, conveniently in the presence of a suitable base, of a quinazoline of the formula II:



II

wherein R^5 , R^6 , Q^1 , X , Y and n are as defined in claim 1 except that any functional group is protected if necessary, and L is a displaceable group, with an alcohol of the formula III



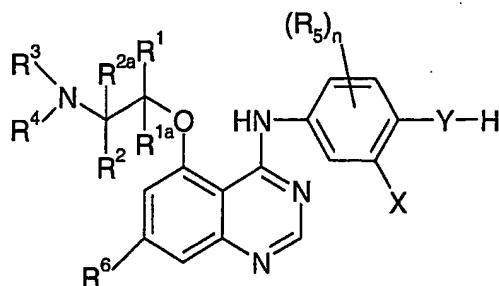
III

10 wherein R^1 , R^{1a} , R^2 , R^{2a} , R^3 and R^4 are as defined in claim 1 except that any functional group is protected if necessary;

or

(b) for the preparation of those compounds of the formula I wherein Y is $OC(R^7)_2$, $SC(R^7)_2$ or $N(R^7)C(R^7)_2$, the reaction, conveniently in the presence of a suitable base, of a quinazoline of

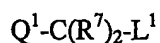
15 the formula IV:



IV

wherein Y is O , S or $N(R^7)$, and X , R^1 , R^{1a} , R^2 , R^{2a} , R^3 , R^4 , R^5 , R^6 , R^7 and n are as defined in claim 1 except that any functional group is protected if necessary, with a compound of the

20 formula V:



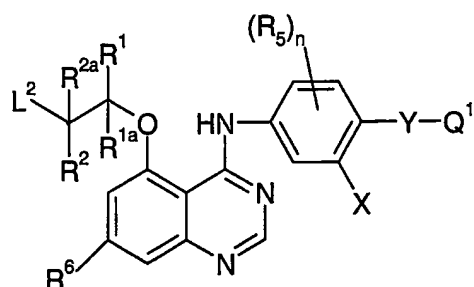
-129-

V

wherein L^1 is a suitable displaceable group and Q^1 and R^7 are as defined in claim 1 except that any functional group is protected if necessary;

or

- 5 (c) the reaction of a quinazoline of the formula VI:



VI

wherein L^2 is a suitable displaceable group and Q^1 , X , Y , R^1 , R^{1a} , R^2 , R^{2a} , R^5 , R^6 and n are as defined in claim 1 except that any functional group is protected if necessary, with an amine of

- 10 the formula VII:

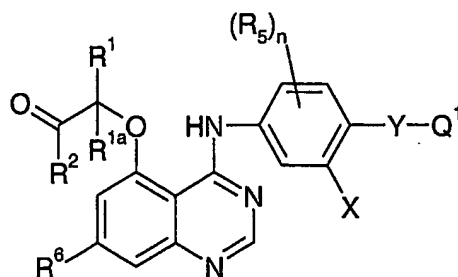


VII

wherein R^3 and R^4 are as defined in claim 1 except that any functional group is protected if necessary;

- 15 or

(d) for the preparation of those compounds of the formula I wherein R^{2a} is hydrogen, the reductive amination in the presence of a suitable reducing agent of the aldehyde or ketone of the formula VIII:



VIII

wherein Q^1 , X , Y , R^1 , R^{1a} , R^2 , R^5 , R^6 and n are as defined in claim 1 except that any functional group is protected if necessary, with an amine of the formula VII:

-130-

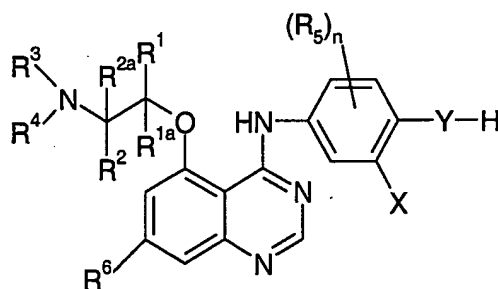
NHR³R⁴

VII

wherein R³ and R⁴ are as defined in claim 1 except that any functional group is protected if necessary;

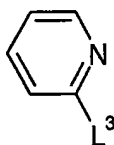
5 or

(e) for the preparation of those compounds of the formula I wherein Y is O or N(R⁷) and Q¹ is 2-pyridyl or 4-pyridyl the reaction, in the presence of a suitable catalyst, of a quinazoline of the formula IV:

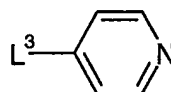


IV

wherein Y is O or N(R⁷) and X, R¹, R^{1a}, R², R^{2a}, R³, R⁴, R⁵, R⁶ and n are as defined in claim 1 except that any functional group is protected if necessary, with an amine of the formula IVa or of the formula IVb:



IVa

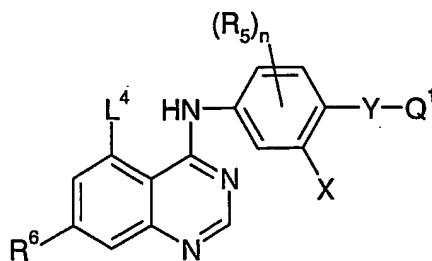


IVb

wherein L³ is a suitable displaceable group;

or

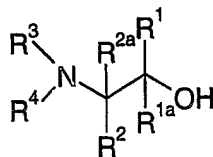
(f) the reaction, conveniently in the presence of a suitable phosphine and a suitable diazo compound, of a quinazoline of the formula II:



II

-131-

wherein R^5 , R^6 , Q^1 , X, Y and n are as defined in claim 1 except that any functional group is protected if necessary, and L^4 is hydroxy, with an alcohol of the formula **III**:

**III**

- 5 wherein R^1 , R^{1a} , R^2 , R^{2a} , R^3 and R^4 are as defined in claim 1 except that any functional group is protected if necessary;
and thereafter, if necessary:
(i) converting a quinazoline derivative of the formula I into another quinazoline derivative of the formula I;
- 10 (ii) removing any protecting group that is present by conventional means;
(iii) forming a pharmaceutically acceptable salt.